REMARKS

Claims 56-73 are pending in the application, claims 56-58 and 68-71 are withdrawn from consideration, claims 59 and 63 have been amended, and claim 74 has been added. Support for the claim amendments and additions may be found throughout the specification, including the claims as originally filed. No new matter has been added.

Amendment of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in any way. Applicants reserve the option to further prosecute the same or similar claims in the instant application, or in a divisional or continuation patent application.

Specification

The specification was objected to as allegedly containing active hyperlinks. According to MPEP 608.01(a), active hyperlinks are those URLs presented between the symbols "< >" or those containing "http://". Applicants have amended the specification to remove any noted occurrences of the "http://" portion of the URLs recited in the specification. Should the Examiner point out any other specific occurrences of active hyperlinks not addressed by the amendments herein, Applicants will be happy to make appropriate correction. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

The specification was objected to for recitation of trademarks in the specification and requested that amendment be made to capitalize the trademarks. Applicants have amended the specification to capitalize any noted occurrences of trademarks recited in the specification. Should the Examiner point out any other specific occurrences of trademarks not addressed by the amendments herein, Applicants will be happy to make appropriate correction. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Rejection of claims 59-67 and 72-73 under 35 U.S.C. §112, first paragraph

Claims 59-67 and 72-73 were rejected under 35 U.S.C. §112, first paragraph, for reasons of enablement. The rejection is respectfully traversed.

The Office Action states that:

> ***A skilled practitioner readily understands that some deviation in any measurable feature exists among normal population. It is not clear and not disclosed in the instant specification, as filed, what the critical level of difference in API-6 is, which is indicative of Alzheimer's disease. It appears that the only numerical information regarding the level of decrease is presented in Table I, page 12, that AFI-21 (which corresponds to API-6), which states that AF-21 was 1.30 fold decreased in CSF of subjects with Alzheimer's.*** (Office Action at 5)

Contrary to the assertions in the Office Action, the specification does sufficiently disclose the critical level of difference in API-6 that is indicative of Alzheimer's disease. In particular, Applicants wish to point out that the data presented in Table I represents the results from 148 subjects having Alzheimer's disease, 60 family members of these Alzheimer's disease subjects, and 32 unrelated controls (see e.g., Example 6, page 122). Samples from each of these subjects was subjected to 2-D gel profiling and statistical analysis (see e.g., Example 6 at pages 132-134). The results of these experiments identified the statistically significant correlation between the level of API-6 and the presence of Alzheimer's disease in a subject. Accordingly, the "single finding" to which the Examiner refers is really a statistically significant compilation of data from a large population of subjects. Furthermore, Applicants also provided additional data supporting the correlation between a decrease in the level of API-6 and Alzheimer's disease in the previously submitted declaration under 37 C.F.R. § 1.132 by Dr. Holly Soares. The declaration presented data showing that over a period of eight years a patient diagnosed with Alzheimer's disease exhibited a precipitous cognitive decline that was associated with a concomitant decrease in the level of API-6. Therefore, Applicants data clearly accounts for any deviation among a normal population and sufficiently discloses a significant correlation between the level of API-6 and Alzheimer's disease.

The Office Action further states that "it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine if other biological samples [e.g., other than CSF] contain API-6, if API-6 are decreased in other

biological samples of subjects with Alzheimer's disease, and what is the level of decrease that is indicative of the diagnosis of Alzheimer's disease." As disclosed in the specification, Applicants identified a correlation between a decrease in the level of API-6 and the development of Alzheimer's disease. In addition to this correlation, Applicants also provide teachings of how to detect API-6 in a biological sample, for example, Table VII (page 40) discloses that there is a commercially available antibody that binds to API-6 (e.g., RDI-CBL159 from Research Diagnostics, Inc.). Additionally, the specification provides teachings as to how to qualitatively or quantitatively detect API-6, for example, by using 2-D gels, immunoassays, western blotting, etc. (see e.g., pages 39-40 and 46-48). These teachings also specify methods to detect API-6 in tissue samples (e.g., a biopsy sample, etc.) or in fluid samples (e.g., CSF, blood, urine, tissue homogenate, etc.). Accordingly, Applicants have provided teachings as to what constitutes a statistically significant decrease of API-6 so as to be indicative of Alzheimer's disease and how to detect API-6 in a variety of biological samples. Clearly, based on the teachings of the specification, it would not be undue experimentation for one skilled in the art to test for the level of API-6 in biological samples such as, for example, blood, urine, tissue homogenate, etc. in subjects with Alzheimer's as compared to a control.

Additionally, the Office Action states that "the instant specification clearly lacks guidance on the subject [of] how to correlate API-6 values with the 'degree of Alzheimer's disease' or 'risk of developing Alzheimer's disease'." Applicants respectfully disagree and submit that the specification provides sufficient guidance as to how to correlate levels of API-6 with a prognosis of Alzheimer's disease. However, in an effort to expedite prosecution of the application, claim 59 has been amended and the amendment is believed to obviate this rejection.

Based on the above remarks, Applicants traverse Examiner's rejections of claims 59-67 and 72-73 under 35 U.S.C. §112, first paragraph. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claim 63 under 35 U.S.C. §112, second paragraph

Claim 63 was rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for recitation of the terms "NCAM" and "other members of the NCAM gene family".

Claim 63 has been amended and the amendment is believed to obviate the rejection. Reconsideration and withdrawal of the rejection is respectfully requested.

Double Patenting

The Office Action indicates that should claim 59 be found allowable, claims 71 and 72 will be objected to under 37 C.F.R. §1.75 as being a substantial duplicate thereof. In particular, the Office Action states that:

> Claim 59 is directed to a method for screening, diagnosis, or prognosis of Alzheimer's disease by detecting API-6, wherein a decreased level of said API-6 relative to a control sample indicates the presence or degree of Alzheimer's disease. Thus, claim 59 obviously encompasses a method of quantitative detection of API-6 as compared to control or a previously determined reference range. Therefore, claims 71 and 72, reciting the same limitations are considered to be covering "the same thing despite a slight difference in wording". (Office Action at 7-8)

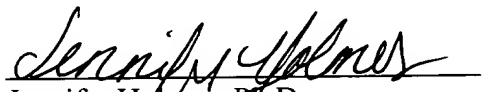
Applicants wish to note that claim 71 has been withdrawn from consideration and believe that the Examiner meant to refer to claims 72 and 73. Accordingly, the potential rejection on double patenting grounds will be addressed with respect to claims 72 and 73.

Contrary to the Examiner's assertion, claim 59 does not "obviously encompass[] a method of quantitative detection of API-6" as recited in claims 72 and 73. Rather, claim 59 is directed, at least in part, to a method of comparing the level of API-6 ***relative*** to that of a control sample or reference range. Such relative comparison would merely entail formation of a ***unitless ratio*** and would not require determination of an absolute quantity. In comparison, a quantitative determination, as recited in claims 72 and 73, would entail determination of an absolute quantity having some form of units attached (such as, for example, mg of protein, volume of a spot/band in a gel, intensity of a spot on a phosphoimager or autoradiogram exposure, etc.). Accordingly, while one aspect of claim 59 may entail forming a ratio after quantitative determination, the claim also encompasses other embodiments which do not require such quantitative determination. Claims 72 and 73 are directed to the specific embodiment which entails quantitative determination. Accordingly, reconsideration and withdrawal of the potential double patenting rejection is respectfully requested.

CONCLUSION

Applicants consider the Response herein to be fully responsive to the referenced Office Action. Based on the above Remarks, it is respectfully submitted that this application is in condition for allowance. Accordingly, allowance is requested. If a telephone conversation with Applicant's Agent would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

By: 
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